UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/534,846	11/21/2005	Alexander Alan Morley	18857	8971

272 7590 12/31/2007

SCULLY, SCOTT, MURPHY & PRESSER, P.C.
400 GARDEN CITY PLAZA
SUITE 300
GARDEN CITY, NY 11530

EXAMINER	
KAPUSHOC, STEPHEN THOMAS	
ART UNIT	**PAPER NUMBER**
1634	

MAIL DATE	DELIVERY MODE
12/31/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/534,846	MORLEY-ET AL.	
	Examiner	Art Unit	
	Stephen Kapushoc	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,10,14,16-25 and 29* is/are rejected.

7)☒ Claim(s) *8,9,11-13,15,26-28,30 and 31* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *13 May 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-31 are pending.

Claims 8, 9, 11-13, 15, 26-28, 30 and 31 are improper multiple dependent claims and are not further examined.

Claims 1-7, 10, 14, 16-25, and 29 are examined on the merits.

Information Disclosure Statement

1. The listing of references in the Search Report (from PCT/AU2003/001497 as submitted on 05/13/2005) is not considered to be an information disclosure statement (IDS) complying with 37 CFR 1.98. 37 CFR 1.98(a)(2) requires a legible copy of: (1) each foreign patent; (2) each publication or that portion which caused it to be listed; (3) for each cited pending U.S. application, the application specification including claims, and any drawing of the application, or that portion of the application which caused it to be listed including any claims directed to that portion, unless the cited pending U.S. application is stored in the Image File Wrapper (IFW) system; and (4) all other information, or that portion which caused it to be listed. In addition, each IDS must include a list of all patents, publications, applications, or other information submitted for consideration by the Office (see 37 CFR 1.98(a)(1) and (b)), and MPEP § 609.04(a), subsection I. states, "the list ... must be submitted on a separate paper." Therefore, the references cited in the Search Report have not been considered. Applicant is advised that the date of submission of any item of information or any missing element(s) will be the date of submission for purposes of determining compliance with the requirements

based on the time of filing the IDS, including all "statement" requirements of 37 CFR 1.97(e). See MPEP § 609.05(a).

It is noted that while the information in the search report pertinent to the Application has been considered, the report has not been treated as an IDS.

Claim Objections

2. Claims 8, 9, 11-13, 15, 26-28, 30 and 31 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only, and cannot depend from any other multiple dependent claim. See MPEP § 608.01(n). Accordingly, the claims 8, 9, 11-13, 15, 26-28, 30 and 31 have not been further treated on the merits.

3. Claim 4 is objected to over recitation of the phrase 'said neoplastic population of cells', where the phrase 'said neoplastic clonal population of cells' is in agreement with the phrase as recited in claim 3, from which claim 4 depends.

Claim 7 is objected to over recitation of the phrase 'said non-neoplastic population of cells', where the phrase 'said non-neoplastic clonal population of cells' is in agreement with the phrase as recited in claim 6, from which claim 7 depends.

Appropriate corrections are required

Claim Rejections - 35 USC § 112 2nd ¶ - Indefiniteness

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-7, 10, 14, 16-25, and 29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 3-7, 10, 14 and 16 are unclear over recitation of 'the subject nucleic acid regions derived from said sample' as recited in claim 1, because the claim does not require any step of obtaining or deriving a subject nucleic acid. As such there is no antecedent basis for 'the subject nucleic acid regions derived from said sample'. See MPEP 2173.05.

Claims 2-7, 10, 14 and 16 are unclear over recitation of 'the subject nucleic acid regions derived from a biological sample' as recited in claim 1, because the claim does not require any step of obtaining or deriving a subject nucleic acid. As such there is no antecedent basis for 'the subject nucleic acid regions derived from a biological sample'. See MPEP 2173.05.

Claims 2-7, 10, 14 and 16 are unclear over recitation of the purpose of the claimed methods for 'diagnosing and/or monitoring a clonal population of cells', as recited in the preamble of claim 2. The methods have only a final step where a level of co-localized nucleic acid is indicative of the presence of a clonal population of cells, where indication of the presence is not 'diagnosing and/or monitoring'. Thus there is not a nexus between the purpose of the method as recited in the preamble and the required methods steps, and as such it is unclear how the required method steps accomplish the purpose of the claimed methods.

Claims 4, 5, 14, and 16 are unclear over recitation of the term 'corresponds', as recited in claim 4, in reference to the relationship between cells and a disease. It is not clear what is required for any cell to 'correspond' to a disease.

Claim 7 is unclear over recitation of the term 'corresponds' in reference to the relationship between cells and a disease. It is not clear what is required for any cell to 'correspond' to a disease.

Claims 17-25 and 39 are unclear over recitation of 'the subject nucleic acid regions derived from a biological sample' as recited in claim 17, because the claim does not require any step of obtaining or deriving a nucleic acid. As such there is no antecedent basis for any 'subject nucleic acid regions derived from a biological sample'. See MPEP 2173.05.

Claims 17-25 and 39 are unclear over recitation of the purpose of the claimed methods for 'diagnosing and/or monitoring a mammalian disease condition', as recited in the preamble of claim 17. The methods have final step wherein only a level of co-localized nucleic acid is indicative of the presence of a clonal population of cells, where indication of the presence is not 'diagnosing and/or monitoring'. Thus there is not a nexus between the purpose of the method as recited in the preamble and the required methods steps, and as such it is unclear how the required method steps accomplish the purpose of the claimed methods.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1-5, 17-20, 23, 24 are rejected under 35 U.S.C. 102(b) as being anticipated by Greiner et al (1995).

Greiner et al teaches the analysis of clonality of T cells in leukemias using PCR and denaturing gradient gel electrophoresis (DGGE).

Regarding claim 1, the reference teaches detecting a clonal population of cells, where the cells are characterized by a diagnostically distinctive nucleic acid region (e.g. the clonal cells have particular T cell receptor (TCR) gene rearrangements; p.47, right col, lns.18-39). The method of Greiner et al comprises co-localizing nucleic acids derived from the subject (Fig. 2; p.49, right col., lns.1-25) in a DGGE analysis, where a DGGE analysis is based on nucleotide sequence identity, and detecting the level of co-localization based on the presentation of a discrete band or a smear on a gel (Fig 5). The refernces teaches that co-localization higher than a background level is indicative of the presence of the clonal cell population (e.g: Fig 5; Fig 7; and p.47, right col., lns. 35-39).

Relevant to claim 2, the methods of Greiner et al, as detailed in the previous paragraph of this Office Action, monitor a clonal population of cells at least in so far as the methods detect the population, where detection is monitoring. Additionally relevant to the limitations of the rejected claim, Greiner et al teaches the analysis of nucliec acids

dervived from a biological sample from a mammal (e.g. p.47, right col., ln.45 – p.48, left col., ln.15).

Regarding claims 3-5, Greiner et al teaches the analysis of cells from acute lymphoblastic leukemia (ALL) samples (relevant to claim 5) (e.g.: p.48, left col., lns.4-9; Fig 5), where ALL samples are neoplastic cells (relevant to claim 3), that correspond to a leukemia (relevant to claim 4).

Regarding claim 17, Greiner et al teaches a method for monitoring ALL (where ALL is a disease condition characterized by a clonal population of cells characterized by diagnostically distinct nucleic acid regions), at least in so far as the methods detect the clonal population of cells, where detection is monitoring. The reference teaches detecting a clonal population of cells, where the cells are characterized by a diagnostically distinctive nucleic acid region (e.g. the clonal cells have particular T cell receptor (TCR) gene rearrangements; p.47, right col, lns.18-39). The method of Greiner et al comprises co-localizing nucleic acids derived from the subject (Fig. 2; p.49, right col., lns.1-25) in a DGGE analysis, where a DGGE analysis is based on nucleotide sequence identity, and detecting the level of co-localization based on the presentation of a discrete band or a smear on a gel (Fig 5). The reference teaches that co-localization higher than a background level is indicative of the presence of the clonal cell population (e.g: Fig 5; Fig 7; and p.47, right col., lns. 35-39).

Regarding claims 18-20, Greiner et al teaches the analysis of cells from acute lymphoblastic leukemia (ALL) samples (relevant to claim 20) (e.g.: p.48, left col., lns.4-

9; Fig 5), where ALL samples are neoplastic cells (relevant to claim 18), that correspond to a leukemia (relevant to claim 19).

Regarding claims 23 and 24, the reference teaches the analysis of T cells, which are immune cells (e.g. p.47, right col., ln.45 – p.48, left col., ln.15).

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 6, 7, 21, and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Greiner et al (1995) in view of Gilliand et al (1991).

Grenier et al teaches methods for detecting a clonal population of cells including all of the limitations of claims 1 and 2, from which rejected claims 6 and 7 depend. Grenier et al teaches methods for diagnosing and/or monitoring a mammalian disease condition including all of the limitations of claim 17, from which rejected claims 21 and 22 depend.

Grenier et al does not specifically teach methods comprising the analysis of a non-neoplastic clonal population (as required for claims 6 and 21), and myelodysplasia (relevant to claims 7 and 22).

Gilliland et al teaches the analysis of non-neoplastic clonal cell populations in that analysis of myelodysplasia.

Relevant to claims 6, 7, 21, and 22, Gilliland et al teaches the analysis of the polymorphic phosphoglycerate kinase (PGK) gene sequence (Fig 1) to determine peripheral blood cell clonality in patients with myelodysplastic syndrome and polycythemia vera (p.6848 – Abstract; Fig 2; Fig 4). The reference teaches analysis of samples from patients with myelodysplastic syndrome and polycythemia vera (relevant to claims 7 and 21), where samples from such patients are non-neoplastic (relevant to claims 6 and 21).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have analyzed the samples and nucleotide sequences of Gilliland et al using the methods as set forth in Greiner et al. One would have been motivated to perform an analysis using the methods of Grenier et al based on the assertion of Grenier et al that such methods allow for the sensitive and accurate detection of sequences in the determination of clonality (p.53, right col., last ¶).

10. Claims 10 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Greiner et al (1995) in view of Enright et al (2000).

Grenier et al teaches methods for detecting a clonal population of cells including all of the limitations of claims 1 and 2, from which rejected claim 10 depends. Grenier et al teaches methods for diagnosing and/or monitoring a mammalian disease condition including all of the limitations of claim 17, from which rejected claim 25 depends.

Grenier et al does not specifically teach methods comprising the analysis of a non-neoplastic clonal population (as required for claims 6 and 21), and myelodysplasia (relevant to claims 7 and 22).

Enright et al teaches the analysis of clonal populations of microorganisms.

Relevant to claims 10 and 25, Gilliland et al teaches the analysis of several polymorphic loci (Table 1 and 2) to determine clonality of methicillin-resistant *S. aureus* isolated from patients (p.1009 - Bacterial isolates). The reference teaches analysis of samples from patients from various patients (Fig 2).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have analyzed the samples and nucleotide sequences of Enright et al using the methods as set forth in Greiner et al. One would have been motivated to perform an analysis using the methods of Grenier et al based on the assertion of Grenier et al that such methods allow for the sensitive and accurate detection of sequences in the determination of clonality (p.53, right col., last ¶).

11. Claims 14, 16, and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Greiner et al (1995) in view of Nomoto et al (2002).

Grenier et al teaches methods for detecting a clonal population of cells including all of the limitations of claims 1-5, from which rejected claims 14 and 16 depend. Grenier et al teaches methods for diagnosing and/or monitoring a mammalian disease condition including all of the limitations of claim 17-20, from which rejected claim 29 depends.

Relevant to claim 16, Greiner et al teaches the use of DGGE, which is an analysis using a denaturing gel electorphoresis.

Grenier et al does not specifically teach methods comprising the analysis of the mitochondrial D loop (as required for claims 14 and 29).

Nomoto et al teaches the analysis of clonal cell populations in hepatocellular carcinoma (HCC).

Relevant to claims 14 and 29, Nomoto et al teaches the analysis of several polymorphic loci in the mitochondrial D loop (Table 1) to determine clonality of HCC cells (p.481 – Experimental design). The reference teaches analysis of samples from patients from various patients (Fig 2).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have analyzed the polymorphic D loop sequences of Nomoto et al in an analysis of ALL by the methods as set forth in Greiner et al. One would have been motivated to examine the nucleotide sequences of Nomoto et al based on the teaching of Nomoto et al (p.481, right col., last ¶) that the high frequency of mutations in the control region of mitochondrial DNA provides a tool to determine the clonal origin of multiple cancers in individual patients.

Conclusion

12. No claim is allowable or free of the teachings of the prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen Kapushoc whose telephone number is 571-272-3312. The examiner can normally be reached on Monday through Friday, from 8am until 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached at 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

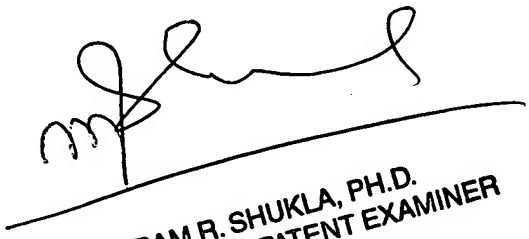
Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days.

Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/Stephen Kapushoc/
Art Unit 1634



RAM R. SHUKLA, PH.D.
SUPERVISORY PATENT EXAMINER